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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,496	10/09/2003	Xiao-Yi Xiao	SYR-HDAC-5003-U	8276
32793	7590	09/30/2005	EXAMINER	
TAKEDA SAN DIEGO, INC. 10410 SCIENCE CENTER DRIVE SAN DIEGO, CA 92121			FREISTEIN, ANDREW B	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 09/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/682,496

Applicant(s)

XIAO, XIAO-YI

Examiner

Andrew B. Freistein

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 1-9 and 11-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 10 and 16-38 is/are rejected.
- 7) ☒ Claim(s) 16-38 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. <u>09222005</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____   |

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### DETAILED ACTION

Claims 1-38 are currently pending in the instant application.

#### *Priority*

This application is claims benefit of US Provisional Application No. 60/419,929, filed 10/21/2002.

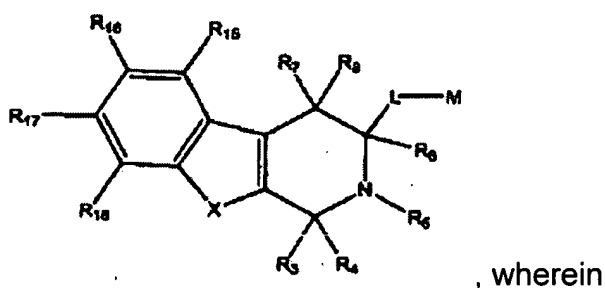
#### *Information Disclosure Statement*

No information disclosure statement (IDS) has been filed to date.

#### *Response to Restriction Requirement*

Acknowledgement is made of Applicant's response to the restriction requirement in a response filed September 22, 2005. Applicant elected Group II, Claims 10 and 16-37. Newly added Claim 38 is joined into Group II.

Additionally, for search purposes applicant elected the compound:

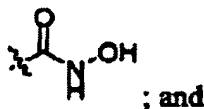


Art Unit: 1626

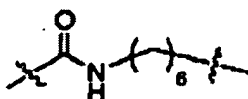
$R_3, R_4, R_5, R_6, R_7, R_8, R_{15}, R_{16}, R_{17}$  and  $R_{18}$  are each hydrogen;

$X$  is  $NR_{14}$ , where  $R_{14}$  is hydrogen;

$M$  is



$L$  is



### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

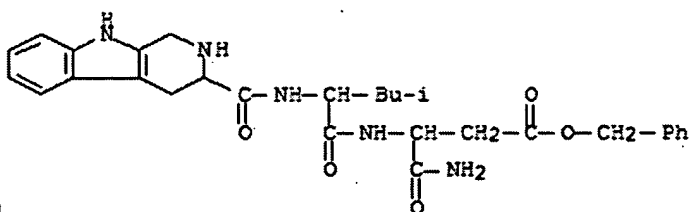
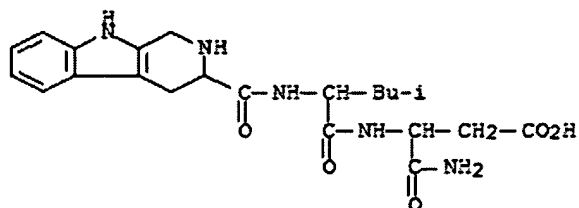
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Molino et al.,

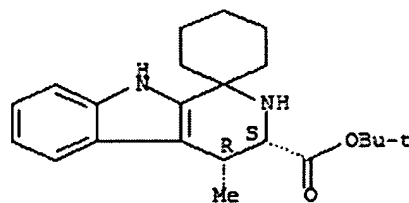
US Pat. No. 5,162,336, disclosing the compounds:

Art Unit: 1626

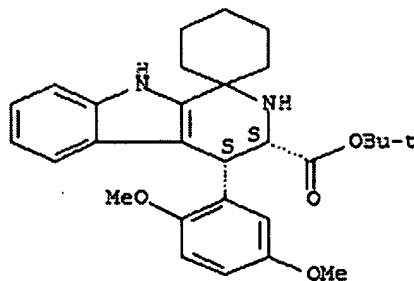
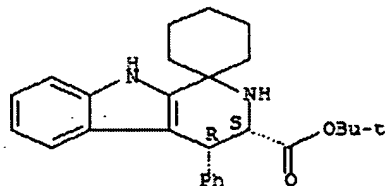
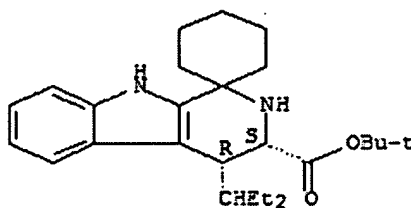
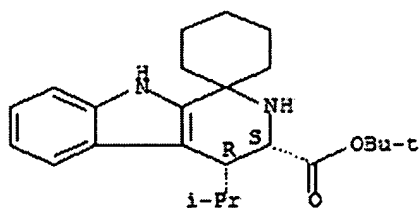


and

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Nemes, et al., Nemes, et al., "A Convenient Synthesis of Conformationally Constrained B-



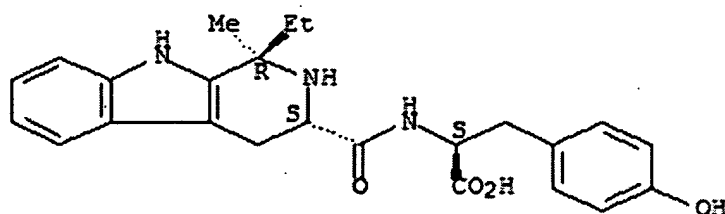
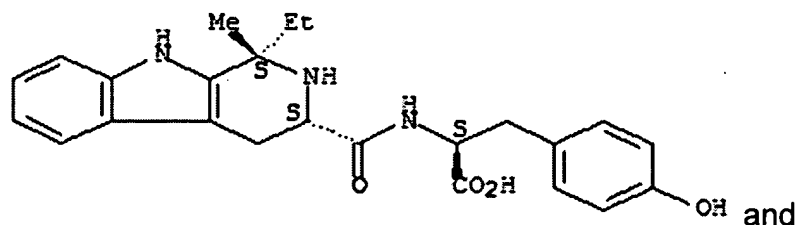
Substituted Tryptophans," disclosing the compounds:



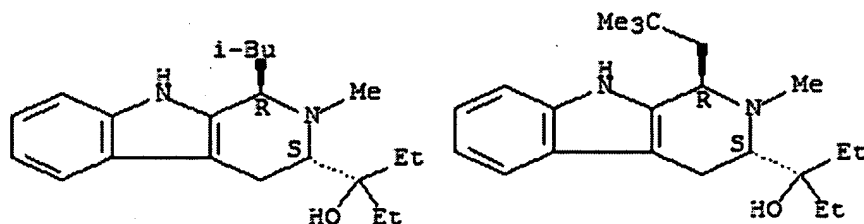
, and

Art Unit: 1626

Claims 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Engel et al., US Pat. No. 5,985,834, disclosing the compounds:

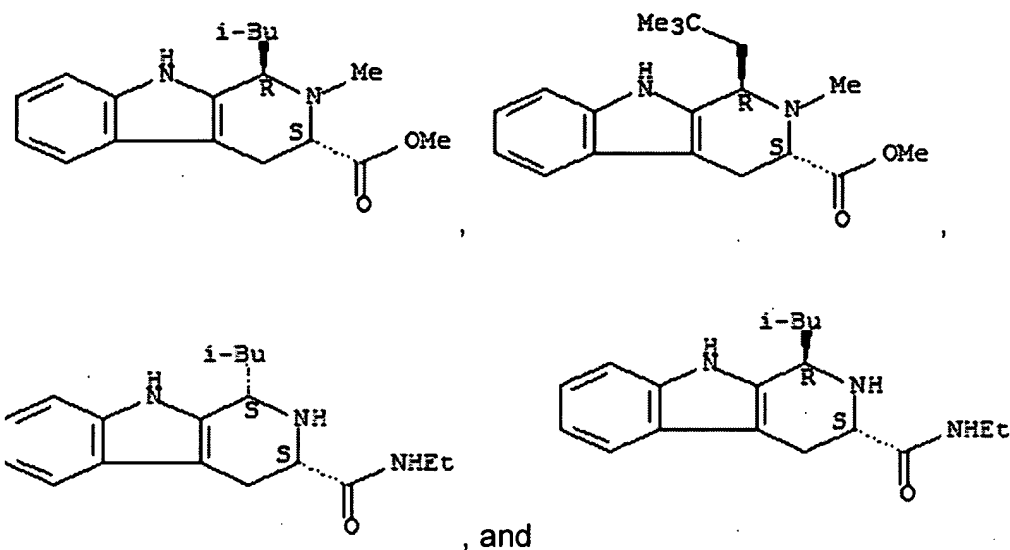


Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by Wei-Min et al., "Chiral Ligands Derived From Abrinbe.3. Asymmetric Pictet-Spengler Reaction of Abrine Methyl Ester and Synthesis of Chiral 1,2,3,4-Tetrahydro-B-carbolines as Promoters in Addition of Diethylzinc toward Aromatic Aldehydes," disclosing the

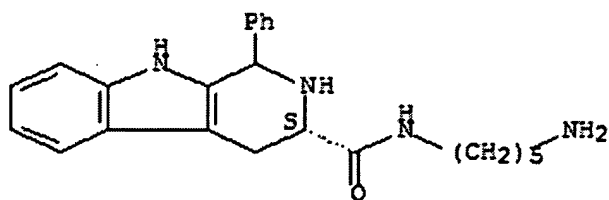


compounds:

Art Unit: 1626

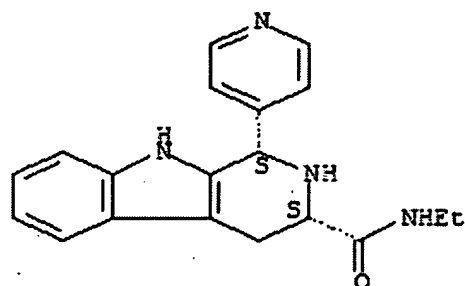


Claims 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang, "Facile Cleavage of the Carbamate Linker of Hydroxymethyl Resin and its Application in Syntheses requiring Strongly acidic Conditions," disclosing the compound:

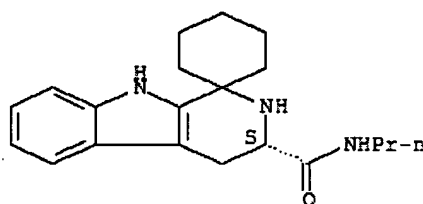


Claims 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang and Guo, "Pictet-Spengler Reaction On Solid Support," disclosing the compound:

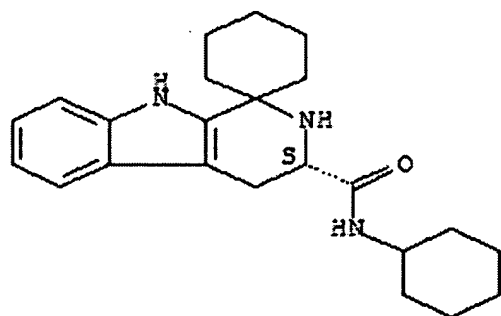
Art Unit: 1626



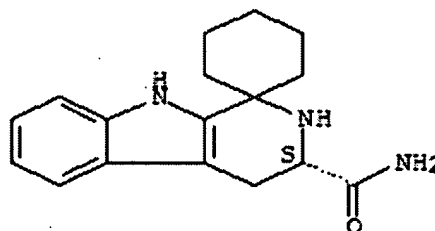
Claims 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by



Levy et al., EP 0466548 disclosing the compounds:



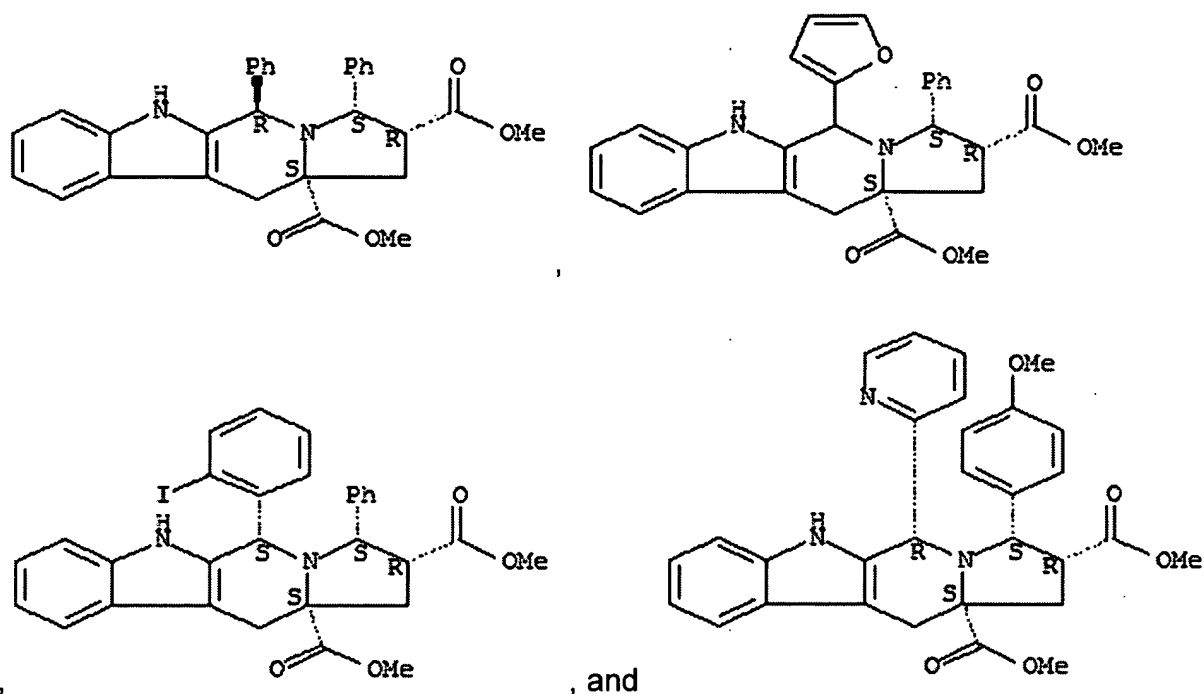
, and



Claims 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by  
Dondas et al., "Sequential 1,3-Dipolar Cycloaddition-Pictet-Spengler Reactions. A  
Versatile Tactical Combination," disclosing the compounds:



Art Unit: 1626



Examiner presumes that the **M** substituent in the above compounds is capable of complexing with a protein metal ion.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10 and 16-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 10 states, "M is a substituent capable of complexing with a protein metal ion; and L is a substituent comprising a chain of 3-12 atoms connecting the M substituent to the carbon atom alpha to the L substituent."

According to the Specification, "M **may be any** substituent that is capable of complexing with a metal ion, and optionally more particularly a zinc ion since a zinc ion is known to be present in the catalytic site of histone deacetylases... **Examples of substituents** capable of complexing with a zinc ion that may be used as the M substituent **include, but are not limited to** trifluoacetyl (-C(O)-CF<sub>3</sub>), -NH-P(O)OH-CH<sub>3</sub>, sulfonamides, [etc]..." (emphasis added) (Spec., p. 27, paragraphs [00114] and [00115]).

Similarly, according to the Specification, "The leader group, L, **may be any substituent** comprising a chain of 3-12 atoms connecting the M substituent to the carbon atom alpha to the L substituent... It is noted that the leader group may comprise **a variety of moieties**, J, that may be used to link the leader group to the remainder of the compound. Synthetic schemes for using these different J moieties to couple the leader group are provided in the **examples**. Beyond these schemes, the particular J moiety **may be widely varied**, depending on the chemistry used to link the leader group to the ring. (emphasis added) (Spec., p. 28, paragraphs [00117] and [00118]).

Moreover, the specification states, "It is noted that the chain of atoms extending between the carbon alpha to the leader group and the M substituent may consist only of carbon atoms. Alternatively, the chain may also comprise non-carbon atoms such as nitrogen, oxygen, and sulfur." (Spec., p. 30, paragraph [00122]).

Exemplification is not an explicit definition. The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision, *Teleflex Inc. v. Ficosa North Am Corp.*, 63 USPQ2d 1374, (Fed. Cir. 2002), *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1854 (Fed. Cir. 2001).

In the instant application, the Specification defines the M and L moieties with general moieties and examples, which does not clearly and unambiguously define the structure of the compounds. As a result, Claim 10 and 16-36 are rejected under 35 U.S.C. 112, 1<sup>st</sup> paragraph for failing to provide an adequate written description of the variables M and L. Claim 37 is rejected for failing to provide a written description of the variable L. Claim 38 is rejected for failing to provide a written description of the variable M.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10 and 16-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Appropriate correction is required.

Claim 18 recites the limitation "further comprises a substituent selected from the group consisting of alkyl, aromatic ring, cyano group, halogen, and carbonyl group." There is insufficient antecedent basis for this limitation in the Claim 10. Claim 18 expands the breadth of R<sup>3</sup> beyond what is claimed in Claim 17 and Claim 10 rather than limiting the scope of the claims upon which Claim 18 depends.

Art Unit: 1626

Additionally, Claim 18 is rejected under 35 U.S.C. 112, second paragraph, because the variables M and L are not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claim 19 recites the limitation "further comprises a substituted or unsubstituted aromatic ring." However, Claim 10 does not define  $R^3$  to further comprise the limitations recited in Claim 19.

Additionally, Claim 19 is rejected under 35 U.S.C. 112, second paragraph, because the variables M and L are not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claims 20-27 are rejected under 35 U.S.C. 112, second paragraph, because the variables M and L are not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claim 28 recites the limitation, " $R^5$  and  $R^6$  are taken together to form...a ring." However, Claim 10 does not provide antecedent basis for  $R^5$  and  $R^6$  to come together to form a ring.

Additionally, Claim 28 is rejected under 35 U.S.C. 112, second paragraph, because the variables M and L are not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claims 29 and 30 recite the limitation, " $R^6$  and  $R^7$  are taken together to form...a ring." However, Claim 10 does not provide antecedent basis for  $R^6$  and  $R^7$  to form a ring."

Art Unit: 1626

Claims 29 and 30 and 31-32 are rejected under 35 U.S.C. 112, second paragraph, because the variables M and L are not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claim 33 recites the limitation "R<sub>7</sub> and R<sub>8</sub> are taken together to form an imine having a substituent R<sub>9</sub>..." However, Claim 10 does not define an imine to be further substituted.

Additionally, Claim 33 is rejected under 35 U.S.C. 112, second paragraph, because the variables M and L are not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claim 34 recites the limitation, "R<sub>7</sub> and R<sub>8</sub> are taken together to form an alkene substituent having the formula =CR<sub>10</sub>R<sub>11</sub> where R<sub>10</sub> and R<sub>11</sub> are each independently selected from a group of substituents consisting of...aryl, alkoxy, alkylamino, arylamino, alkylthio, acylamino, sulfonylamino, [or] a carbonyl group." However, such a definition is chemically unstable.

Additionally, Claim 34 and Claims 35-36 are rejected under 35 U.S.C. 112, second paragraph, because the variables M and L are not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claim 37 is rejected under 35 U.S.C. 112, second paragraph, because the variable L is not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Art Unit: 1626

Claim 38 is rejected under 35 U.S.C. 112, second paragraph, because the variable M is not properly defined so as to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

### ***Status of the Claims***

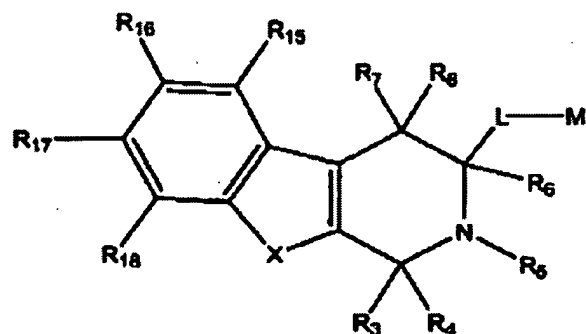
Claims 1-38 are currently pending in the instant application.

Claims 10 and 16-38 (in part) and 1-9, 11-15 are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions under 37 CFR § 1.142(b). The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. In addition, a reference that anticipates one invention would not render obvious the other invention.

### ***Elected and Examined Subject Matter***

The scope of the invention of the elected subject matter and the examined subject matter is as follows:

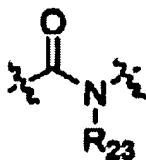
Compounds of the Formula of Claim 10,



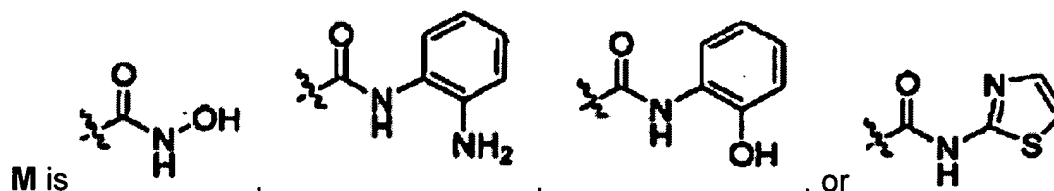
, wherein according to the claims:

R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>15</sub>, R<sub>16</sub>, R<sub>17</sub> and R<sub>18</sub> are each independently Hydrogen or C<sub>1-4</sub>alkyl;

Art Unit: 1626

X is NR<sub>14</sub>;R<sub>14</sub> is Hydrogen or C<sub>1-4</sub>alkyl;

L is

R<sub>23</sub> is C<sub>1-10</sub>alkyl; and

M is

As a result of the election and the corresponding scope of the invention, identified supra, the remaining subject matter of Claims 1-36 and 60-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups such as furan, thiofuran, pyrrole, isoimidazole, pyrazine, benofuran, isoquinoline, cinnoline, etc. which are chemically recognized to differ in structure, function, and reactivity.

Therefore, the subject matter which was withdrawn from consideration as being non-elected subject matter materially differs in structure and composition from the examined subject matter so that a reference which anticipates the examined subject matter would not render obvious the non-elected subject matter.

### ***Claim Objections***

Claims 16-38 are objected to as being dependent claims of rejected base claims.

Claims 37 and 38 are rejected for containing non-elected subject matter.

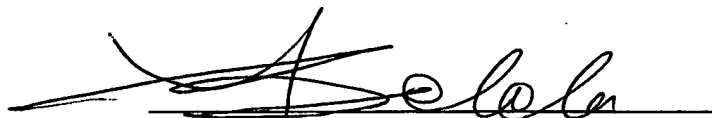
***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Andrew B. Freistein  
Patent Examiner, AU 1626



Taofiq Solola, Ph.D., J.D.  
Primary Patent Examiner, AU 1626  
Date: September 22, 2005